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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
SHEINBERG, MONIKA B	
ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 03/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/912,968	DOTSON ET AL.	
	Examiner	Art Unit	
	Monika B Sheinberg	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 September 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *35-50* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *35-50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Detailed Action.*

DETAILED ACTION

Election/Restrictions

1. Applicant's election of Group I (claims 35-50 as directed to SEQ ID NO: 2 and 7) with traverse in the response filed September 30, 2003 is acknowledged. The traversal is on the ground(s) that

> "the Examiner has not shown that a search and examination of the entire application would cause a serious burden[...] Applicants believe no serious burden would result by the search and examination of the 5 untranslated sequences (SEQ ID NO: 2, 5, 32, 33, and 35). Applicants disagree that each nucleotide sequence and its corresponding oligonucleotides in the application is necessarily a patentably distinct species[...]" (p. 3)

This is not found persuasive because SEQ ID NO: 2, 5, 32, 33 and 35 are completely distinct sequences. A prior art search of SEQ ID NO: 2 and its corresponding subsequences would not necessarily be relevant to the art of the other sequences. In addition, the size of sequence databases has increased over the past years significantly, thereby presenting a significant burden to search multiple sequences in the sequence databases. Further, the claims are directed to a single sequence of the five to be the second transgenic nucleic acid molecule. The requirement is still deemed proper and is therefore made FINAL.

1. With respect to the sequences directly corresponding to SEQ ID NO: 2, SEQ ID NO: 8, 9 and 28 of SEQ ID NO: 2 have been rejoined with the instant claims.

2. Applicant is requested to amended the claims to reflect the elected invention.

3. Claims 35-50 as directed to SEQ ID NO: 2, 7, 8, 9 and 28, are hereby examined.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claim 50 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described

in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

6. The claim is directed to encompass nucleic acid sequences that are not limited to SEQ ID NO: 2, 7-9 and 28. Claim 50 encompasses any sequences that are at most described as the 3'-untranslated sequence from the 3' end of the *Pisum sativum* rbcS E9 gene. Thus as the claim is written the sequences encompassed by the claim extend in both directions from SEQ ID NO: 2, 7-9 and 28 (7-9 and 28 are of SEQ ID NO: 2), and it encompasses sequences of any magnitude and/or content that comprise at least a 3'-untranslated sequence from the 3' end of the *Pisum sativum* rbcS E9 gene. These sequences correspond to sequences from other species, mutated fragment sequences, allelic variants, splice variants, genomic sequences and so forth. Thus the claim encompass an extremely large genus of polynucleotides, wherein the specification's disclosure of a single sequence of SEQ ID NO: 2 is not representative of this genus. None of these additional sequences encompassed by the broadly claimed genus meet the written description provision of 35 USC 112, first paragraph. The specification provides insufficient written description to support the genus encompassed by the claim.

7. The claim language "hybridize" (claim 50) does not present the conditions claimed (high, moderate, or low stringency); thus encompassing sequences that again correspond to sequences from other species, mutated fragment sequences, allelic variants, splice variants, genomic sequences and so forth. In the instance that high stringency may be indicated to be intended, it is to be noted that even sequences that hybridize under high stringency would tolerate some mismatches, which thus results in the claim encompassing sequences that again correspond to sequences from other species, mutated fragment sequences, allelic variants, splice variants, genomic sequences and so forth. None of these additional sequences encompassed by the broadly claimed genus meet the written description provision of 35 USC 112, first paragraph. The specification provides insufficient written description to support the genus encompassed by the claim.

8. *Vas-Cath Inc. v. Mahurkar*, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons

of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116.)

9. The skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC 1993) and *Amgen Inc. V. Chugai Pharmacentical Co. Ltd.*, 18 USPQ2d 1016. In *Fiddes v. Baird*, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided the bovine sequence.

10. Finally, *University of California v. Eli Lilly and Co.*, 43 USPQ2d 1398, 1404, 1405 held that:

> ...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.* , 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); *In re Gosteli* , 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood* , 107 F.3d at 1572, 41 USPQ2d at 1966.
>
> An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. *Fiers v. Revel*, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id. at 1170, 25 USPQ2d at 1606.

Accordingly, the specification does not provide a written description of the invention of claim 50.

11. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

12. Claims 35-49 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

13. Claim 35 is vague and indefinite due to the lack of clarity in the steps of methodology due to the claim language and the arrangement of the claim language. It is unclear whether the "method comprising" is directed to merely to mRNA of condition (b) or is directed to both condition (a) and (b). As currently written it appears that the steps of providing complementary DNA, amplification, and hybridization are carried out in order to make the non-detectable mRNA of condition (b) to the level of 'detectable' as in condition (a).

> *Claim 35. A method to detect expression of a first transgenic nucleic acid molecule in a sample having* either (a) a detectable amount of mRNA transcribed from a second transgenic nucleic acid molecule or (b) a substantially non-detectable amount of said mRNA, *said method comprising providing a complementary DNA of the mRNA, amplifying said complementary DNA and hybridizing said complementary DNA with at least one oligonucleotide designed to hybridize to said second transgenic nucleic acid molecule, whereby said hybridizing indicates the expression of said first transgenic nucleic acid molecule in the sample.*

Another interpretation is the following:

> *Claim 35.* A method to detect expression of a first transgenic nucleic acid molecule in a sample having either
>
> a) a detectable amount of mRNA transcribed from a second transgenic nucleic acid molecule or
> b) a non-detectable amount of said mRNA,
>
> said method comprising
>
> i. providing a complementary DNA of the mRNA
> ii. amplifying said complementary DNA
> iii. hybridizing said complementary DNA with at least one oligonucleotide designed to hybridized to said second transgenic nucleic acid molecule
>
> whereby said hybridizing indicates the expression of said first transgenic nucleic acid molecule in the sample.

Wherein the steps i-iii are directed to either step (a) or (b). As such, claims 36-49 are indefinite due to their dependency from claim 35.

14. Claim 35 is vague and indefinite due to the lack of clarity of the method steps that perform the method claimed. It is unclear whether the method claimed is directed to detecting DNA that corresponds to the 2nd transgenic nucleic acid; detecting the expression of the 2nd transgenic nucleic acid; detecting the presence or absence of the 1st transgenic nucleic acid molecule; or detecting the expression of 1st transgenic nucleic acid molecule. Although the preamble sets forth the intention to be detecting the expression of the 1st transgenic nucleic acid

molecule, the method steps are merely detecting DNA that corresponds to the 2nd transgenic nucleic acid molecule.

> Claim 35. A method to detect expression of a first transgenic nucleic acid molecule in a sample having either (a) a detectable amount of mRNA transcribed from a second transgenic nucleic acid molecule or (b) a substantially non-detectable amount of said mRNA, said method comprising providing a complementary DNA of the mRNA, amplifying said complementary DNA and hybridizing said complementary DNA with at least one oligonucleotide designed to hybridize to said second transgenic nucleic acid molecule, whereby said hybridizing indicates the expression of said first transgenic nucleic acid molecule in the sample.

It is unclear as to what is the complementary DNA being provided. There is a disconnect between the method intended and the method claimed which appears to be of two separate methods: the preamble is a method of detecting transgenic nucleic acids, while the body of the claim is a method of detecting complementary DNA by oligonucleotide hybridization. As the claim is currently written steps (i)-(iii) are not required to occur within the same test tube due to the complementary DNA of the mRNA being "provided". If the complementary DNA is provided then the actual transgenic mRNA need not ever be there. The amplification step is only of the "provided complementary DNA" and not of complementary DNA created directly from the mRNA within the sample. The hybridization step is of an oligonucleotide to the "provided complementary DNA"; again not to complementary DNA created directly from the mRNA within the sample. As instantly claimed, the oligonucleotide is hybridizing to a provided set of complementary DNA which does not have any direct correlation to second transgenic mRNA aside from having a complementary sequence (which in itself is not
As such, claims 36-49 are indefinite due to their dependency from claim 35.

15. Claims 40, 43 and 44 are vague and indefinite due to lack of clarity of the terms "substantial identity" (claims 43 line 2), and "substantially identical" (claim 44 line 2; claim 40 line 2). A possible interpretation is that a substantially identical sequence must be of the same length and be the full and exact complement of the recited sequence. Another interpretation is that a substantial identity is meant to include those sequences with less than 100% complementarity, such as 90%, 50%, or even 10%. Therefore the metes and bounds of the claim are unclear because the specification has not defined how much identity a nucleic acid must have to be considered "substantially identical." In addition, please note that although the sequence of claim 43 is directed to a consecutive 100bp sequence, the use of the word consecutive is

contradicted by stating that the sequence only have "substantial identity"; thus it is no longer a consecutive sequence of the elected sequence SEQ ID NO: 2.

> "[...]comprises at least 100 base pairs of consecutive sequence having substantial identity to a sequence selected from" (lines 2-3).

The same is true of claims 44:

> "15 bases substantially identical or complementary to a consecutive sequence selected from" (line 2).

16. Claim 47 is vague and indefinite due to the lack of clarity of the claim language (emphasis added) "said at least one oligonucleotide comprises a primer **pair and a probe** designed to hybridize to a **[/any]** nucleic acid molecule in a 5' nuclease assay" lines 1-2. As written, the claim appears to require that the oligonucleotide be made up of all three of these sequences as one long sequence – the forward primer, the reverse primer, and the probe – and hybridize to any nucleic acid molecule. The claim could also be interpreted to encompass two separate primers and a separate probe oligonucleotide. However due to the wording, it is unclear what is intended by the claimed recitation.

Claim Rejections - 35 USC § 102

17. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

18. Claims 35, 36, 40-42, 44-47 are rejected under 35 U.S.C. 102(a) as being anticipated by Miyamoto et al. (*Plant Molecular Biology Reporter*, June-2000).

Miyamoto et al. teaches a method of quantitating very low levels of mRNA expression of a transgenic nucleic acid (beta-glucuronidase: GUS) (*claim 36*)(p. 101, *Introduction*, 1st paragraph). The method of quantitation is carried out by RT-PCR (claim 41), specifically quantitative RT PCR (*claim 42*) (p.102, 2nd paragraph). Page 102 (*Primers and a fluorogenic probe for RT-PCR*) describes a primer pair and a probe for the oligonucleotides utilized in the method

(*claim 47*). (Note: The claim language "designed to hybridize to a nucleic acid molecule in a 5' nuclease assay" in claim 47 line 2, is not given patentable weight due to an intended use that does not occur in the method claimed. In addition, the oligonucleotide need only be "designed" to hybridize to the mRNA, this does not indicate that it is within the sample and hybridizing to the mRNA, merely it is capable of doing so if in the same sample.) The method of RT-PCR is the use of reverse transcriptase to amplify and generate complementary DNA of the targeted mRNA, to which at least one oligonucleotide can hybridizes and thereby detect the expression of the transgenic nucleic acid molecule (*claim 35*)(p. 104, *RT-PCR*). The oligonucleotides provided as the primers and probe for the RT-PCR on page 102 have a sequence of substantial identity to a molecule of SEQ ID NO: 7 as seen below (*claim 40*).

SEQ ID NO: 7 CACGTTC**GT**CAA**GTTCAAT**GC
Sense primer TACGGCAAA**GT**GTGGG**TCAAT**AATCA

The sense primer which has substantial identity to SEQ ID NO: 7 (which is a subsequence of SEQ ID NO: 2), comprises at least 15 bases (*claim 44*). The probe of the reference is a fluorogenic probe, thus has a detectable label (*claim 45*), which is a fluorescent label (*claim 46*).

19. Claims 35, 40, 41, 47 and 49 are rejected under 35 U.S.C. 102(b) as being anticipated by Hamilton et al (*Gene*, 1997).

Hamilton demonstrates the expression of transgenes in a BIBAC vector (p. 113, 2nd column, 3rd paragraph), wherein a successful transfection into the host plant is determined based upon the following transgenic nucleic acids: *sacB* gene, GUS-NPTII gene (beta-glucuronidase – neomycin phosphotransferase II), and the HYP gene (hygromycin phosphotransferase). In one example, the first transgenic nucleic acid is the *sacB* gene and the second transgenic acid is the GUS-NPTII and/or HYG gene:

> Potential transgenic plants were initially tested by PCR using primers to the GUS-NPTII and HYG [...]. [...] Plants that tested positive for the BIBAC T-DNA by PCR [*thereby amplification, claim 35 step ii, and claim 41*] were all verified by Southern analysis [*thereby hybridization, claim 35 step iii, and claim 49*] using a NPTII specific probe. (p. 113, 1st column, 3rd paragraph)(see also figure 3).

As such, the method includes a primer pair and probe (*claim 47*). (Note: The claim language "designed to hybridize to a nucleic acid molecule in a 5' nuclease assay" in claim 47 line 2, is not given patentable weight due to an intended use that does not occur in the method claimed. In

addition, the oligonucleotide need only be "designed" to hybridize to the mRNA, this does not indicate that it is within the sample and hybridizing to the mRNA, merely it is capable of doing so if in the same sample.) The claimed oligonucleotides, primers and probe SEQ ID NO: 7, 8, 28 and 9 (*claim 40*), are considered functionally equivalent to any primers/probe that would detect the transgenic sequence taught by Hunt absent secondary evidence; the primers/probe would especially detect those sequences which are only "substantially" identical. A second example of the method demonstrated is wherein the first transgenic nucleic acid corresponds to large DNA inserts into the BIBAC1 and BIBAC2 plasmids. The second transgenic nucleic acid corresponds to the GUS-NPTII. Hamilton demonstrates in "[f]igure 4b and c shows the hybridization of BIBAC DNA to a GUS-NPTII-specific probe and a HYG-specific probe, respectively" (p. 113, 2nd column, 2nd paragraph).

Claim Rejections - 35 USC § 103

20. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the

various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

21. Claims 35-50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hunt et al (*DNA*, 1988) in view of Freeman et al. (*Biotechniques,* 1999).

Hunt et al demonstrates the transformation of a tobacco plant with a plasmid carrying the 3'noncoding strand of the pea rbcS-E9 3'region (*claims 37, 38*) which aligns 99.5% with SEQ ID NO: 2 (a 637 bp sequence) from residue 1-633 (*claim 39*), and a desired transgene pAH10 (figure 2A). Due to claim 39 reciting the phrase "has a sequence selected from" (line 2), the claim comprises fragments and sequences greater and smaller than the elected sequence comprising such fragments. For example, this encompasses even a two nucleotide sequence of SEQ ID NO: 2 since a fragment remains inclusive of a sequence of shorter length with each base pair matched with the base pairs of the elected sequence. (An amendment to the claim language to recite, "has **the** sequence selected from" is suggested). The reference further teaches the oligonucleotides of claims 40 and 44 wherein SEQ ID NO: 7, 9, 8 (which align at residues 27-49, 51-76, and 77- 102 respectively) are encompassed by the sequence displayed in figure 2. The rbcS region is representative of the 2nd transgenic nucleic acid as per claim 35 and the pAH10 is the 1st transgenic nucleic acid. In addition, the indicated region has greater than 15 and greater than 100 contiguous base pairs that are substantially identical to SEQ ID NO: 2 (*claims 43, 44*). Hunt detects the rbcS by the S1 nuclease assay (p. 331, 1st –2nd column, *RNA isolations and S1 nuclease protection analysis*) where in Klenow was utilized (therefore amplification) for radiolabeling the oligonucleotides with radiolabels such as [alpha-32P]dATP or dCTP as required by claims 45 and 46; and probes were hybridized (claim 35) to the rbcS region for protection during the S1 nuclease thereby detecting the 2nd transgenic nucleic acid and the 1st transgenic nucleic acid.

Hunt does not teach the amplification by PCR or RT-PCR, quantitative and competitive RT-PCR, the primers utilized for the amplification as required by claims 36, 41, 42, 47, 48 and 50.

Freeman teaches the benefits of PCR, specifically utilizing quantitative RT-PCR, both competitive and non-competitive (pp. 116-117) to quantify mRNA (*claims 36, 41, 42*).

> Reverse transcription PCR (RT_PCR) represents a sensitive and powerful tool for analyzing RNA. [abstract]. No other techniques offers the potential to rapidly and quantitatively analyze a number of gene products from multiple small samples in a multiplex format. (p. 122, 3rd column, last paragraph).

On page 113, Freeman teaches designing primers for the use in such an assay to be gene specific or non-specific however if specific then it "increases specificity and decreases background associated with other types of primers" (3rd column, 1st – 2nd paragraph). Means of detecting the amplified products are taught to be hybridization based assays such as Southern Blots or fluorescence detection (p. 114, 2nd column, 1st paragraph). Sequence specific probe design for detection of the amplified products is taught on page 114 (2nd column, 2nd paragraph), wherein the probe has a detectable fluorphoric label.

Thus, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention was made to improve the detection method of Hunt et al and further modify the mRNA expression analysis to utilize quantitative RT-PCR which includes amplification along with primers and probes designed for quantitative RT-PCR as per the teachings of Freeman et al. because Freeman teaches that quantitative RT-PCR provides increased sensitivity in mRNA detection. With regard to claim 39 and the sequence of the second transgenic nucleic acid, the claim comprises fragments and sequences greater and smaller than the elected sequence comprising such fragments thus it encompasses even a two nucleotide sequence of SEQ ID NO: 2 since a fragment remains inclusive of a sequence of shorter length with each base pair matched with the base pairs of the elected sequence. With regard to the oligonucleotides (primers/ probes) of claim 40, it would have been further *prima facia* obvious to one of ordinary skill in the art to design primers and probes for use in the method of Hunt in view of Freeman. The ordinary artisan would be motivated to generate probes and primers for the improved method of RNA detection of Hunt in view of Freeman, and in doing so, would generate a number of probes and primers including those with SEQ ID NO: 7, 8, 9 and 28 for use in the RNA detection

method of Hunt and Freeman. These sequences are considered functionally equivalent in carrying out the amplification and detection step in the RT-PCR method for detection the 3'noncoding strand of the pea rbcS-E9 3'region of Hunt in view of Freeman, absent secondary considerations. An ordinary artisan would have been motivated to use quantitative RT-PCR amplification process instead of the S1 nuclease assay in the detection method of Hunt et al, for increased specificity and decreased background as per the teachings of Freeman et al. [As shown above, the primers and probes, SEQ ID NO: 7, 9, 8, align at residues 27-49, 51-76, and 77- 102 respectively]. One of ordinary skill in the art would have been motivated to do RT-PCR RNA analysis taught by Freeman et al due to the advantages of improved RNA analysis and detection because:

> Reverse transcription PCR (RT_PCR) represents a sensitive and powerful tool for analyzing RNA. [abstract]. No other techniques offers the potential to rapidly and quantitatively analyze a number of gene products from multiple small samples in a multiplex format. (p. 122, 3rd column, last paragraph).

Specification Objections

22. The disclosure is objected to because it contains embedded hyperlinks and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code in the specification in the following place: a) page 11, lines 9-10; b) page 38, line 10; and elsewhere in the specification. See MPEP § 608.01.

23. In addition, the specification is objected to due to the inconsistency in the specification for the description as to that which describes SEQ ID NO: 2 and 3. Table 1 describes SEQ ID NO: 2 as being the 3'untranslated region of *Pisum sativum* rbcS gene, while SEQ ID NO: 3 is a NPTII gene (kanamycin resistance). This contradicts that which Example 1 (pp. 37-38) describes, wherein SEQ ID NO: 3 is the 3'untranslated region of *Pisum sativum* rbcS gene (p. 37, lines 22-23). Clarification is requested.

Conclusion

- Claim 50 is rejected under 35 U.S.C. 112, first paragraph – written description.
- Claims 35-49 are rejected under 35 U.S.C. 112, second paragraph.

- Claims 35, 36, 40-42, 44-47 are rejected under 35 U.S.C. 102(a) as being anticipated by Miyamoto et al.
- Claims 35, 40, 41, 47 and 49 are rejected under 35 U.S.C. 102(b) as being anticipated by Hamilton et al.
- Claims 35-50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hunt et al. in view of Freeman et al.
- Objection to the specification.

No claim is allowed.

Inquiries

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR § 1.6(d)). The central **Fax number is (703) 872-9306**.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Monika B. Sheinberg, whose telephone number is (571) 272-0749. The examiner can normally be reached on Monday-Friday from 9 A.M to 5 P.M. If attempts to reach the examiner by telephone are unsuccessful, the primary examiner in charge of the prosecution of this case, Jehanne Sitton, can be reached at (571) 272-0752. If attempts to reach the examiners are unsuccessful, the examiner's supervisor, Gary Benzion, can be reached at (571) 272-0782.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to Patent Analyst, Chantae Dessau, whose telephone number is (571) 272-0518, or to the Technical Center receptionist whose telephone number is (703) 308-0196.

March 16, 2004
Monika B. Sheinberg
Art Unit 1634

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